**Title:** Independent and joint associations of grip strength and adiposity with all-cause and cardiovascular disease mortality in 403,199 adults: The UK Biobank study

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**Short running head**: Grip strength, adiposity and mortality

**Abbreviations**: BMI, body mass index; CVD, cardiovascular disease; GS, grip strength; HR, hazard ratio; MVPA, moderate-to-vigorous physical activity; %BF, percent body fat; WC, waist circumference

## Abstract

**Background:** Higher grip strength (GS) is associated with lower mortality risk. However, whether this association is independent of adiposity is uncertain.

**Objective:** The purpose of this study was to examine the associations between GS, adiposity and mortality.

**Design:** The UK Biobank study is an ongoing prospective cohort of >0.5 million UK adults aged 40-69 years. Baseline data collection (2006-2010) included measurements of GS and adiposity indicators including body mass index (BMI). Age- and gender-specific GS quintiles were used. BMI was classified according to clinical cut-points.

**Results:** Data from 403,199 participants were included in analyses. Over a median 7.0-year follow-up, 8,287 all-cause deaths occurred. The highest GS quintile had 32% (95% confidence interval [CI]: 26%, 38%) and 25% (95% CI: 16%, 33%) lower all-cause mortality risks in men and women, respectively, compared with the lowest GS quintile, after adjustment for confounders and BMI. Obesity class II (BMI≥35) was associated with greater all-cause mortality risks. Compared with the highest GS and normal weight category, the highest GS and Obesity class II category showed relatively higher all-cause mortality hazards (not statistically significant in men); however, the increased risk was relatively lower than the risk for the lowest GS and Obesity class II category. All-cause mortality risks were generally lower for obese but stronger individuals than for non-obese but weaker individuals. Similar patterns of associations were observed for cardiovascular mortality.

**Conclusions:** Lower grip strength and excess adiposity are both independent predictors of higher mortality risk. The higher mortality risk associated with excess adiposity is attenuated, although

not completely attenuated, by greater GS. Interventions/polices should focus on improving muscular strength of the population regardless of their adiposity levels.

Key words: grip strength, adiposity, muscle strength, obesity, mortality, UK Biobank

## Introduction

Obesity is a global public health concern (1). Excess adiposity is known to be associated with greater risk of mortality as well as cardiovascular disease (CVD) such as heart failure, hypertension, and coronary heart disease (2). However, substantial evidence (3) suggests greater aerobic fitness can lower the risk of death and CVD associated with greater fatness. Muscular fitness, a complementary aspect of fitness, has also been found to be a strong predictor of mortality (4). As such, grip strength (GS), as a simple inexpensive measure of overall muscular strength (5-7), has been recognized as a useful prognostic indicator of mortality (8, 9) as well as adverse health outcomes, such as sarcopenia and frailty (10). A few studies (11-14) have attempted to further explore the "fit-fat" paradigm in relation to mortality and muscle strength, suggesting that mortality risk may be reduced in individuals with higher muscle strength irrespective of weight status. However, the evidence on the associations of muscle strength and fatness with mortality has been predicated primarily upon data with a relatively small sample size (<8000) of men (11, 12) or older adults (13). So, findings from these studies provide limited evidence on the relative risk of mortality for the combination of muscle strength and fatness for general adult populations. Furthermore, the majority of the studies have used body mass index (BMI) as a sole crude adiposity indicator (12-14). Abdominal adiposity defined by waist circumference (WC) predicts mortality independently of general adiposity (i.e. BMI, percent body fat [%BF]) (15). Hence, it is critical to discern the interactions of different adiposity indicators and muscle strength with mortality in general populations of men and women. Therefore, the purpose of the present analysis is to examine the relative risk of all-cause and CVD mortality for GS, various clinical adiposity measures (BMI, WC, %BF) and their interactions in middle-aged and older men and women.

## Subjects and Methods

### Study design and participants

UK Biobank is an ongoing UK national cohort of over half a million adults aged 40-69 years at recruitment. Individuals were contacted who were registered with the National Health Service and living <25 miles away from one of 22 assessment centers across the UK. Of those, >500 000 individuals performed baseline data collection (2006-2010) that included a wide variety of physical measurements and biological samples, as well as questionnaires on socio-demographic factors, family history/early-life exposures, general health/disabilities, environmental/lifestyle factors, and psychological/cognitive state. The UK Biobank methodology is described in detail elsewhere (16). All participants signed informed written consent prior to participation, and the protocol of the UK Biobank project was approved by the North West Multi-Centre Research Ethics Committee.

### Exposures

#### *Grip strength (GS)*

GS was assessed once in each hand using a Jamar J00105 hydraulic hand dynamometer, which can measure isometric grip force up to 90 kilograms (calibrated by staff at the start of each measurement day) showing good reliability and reproducibility (17). The handle of the device was adjustable to five grip positions between 1-3/8 and 3-3/8 inches. Participants were allowed to choose a grip position that they felt most comfortable with. Each participant was asked to grasp the handle of the device in their right hand while sitting upright on a chair with their forearm on the armrest. They were required to maintain a 90° angle of their elbow adjacent to their side so that their thumb would face upwards while squeezing the handle as strongly as possible for about 3 seconds. The same protocol was undertaken with the left hand. For the

current analysis, values from the two hands were averaged if available; otherwise, the value from a single hand was used in a small subsample (n=1,177).

***Adiposity measures***

BMI was calculated as measured weight (kg) divided by measured height (m) squared. WC was measured using a tape measure at the level of the umbilicus. Fat-free mass was assessed with the Tanita BC-418MA bio-impedance analyzer, from which %BF was calculated as 1 minus fat-free mass divided by body weight. BMI was categorized into normal weight (18.5-24.9 $kg/m^2$), overweight (25.0-29.9 $kg/m^2$), obesity class I (30.0-34.9 $kg/m^2$) and obesity class II (≥35.0 $kg/m^2$). The following sex-specific clinical cut-offs were applied to create three groups of WC and %BF: WC<94cm, 94-102cm or ≥102cm for men; WC<80cm, 80-88cm, or ≥88cm for women (1); %BF≤20%, 20-25% or >25% for men; and %BF≤30%, 30-33% or >33% for women (18).

**Outcomes**

Participants were followed up for mortality until February 15$^{th}$ 2016 through linkage with death records from the National Health Service Information Centre and the Scottish Morbidity Record. CVD mortality was defined as the International Classification of Diseases-10 codes F01 and I00-I99. The median follow-up period was 7 years (interquartile range: 6.3 and 7.6 years).

**Covariates**

The following variables that could confound GS-mortality associations were included as covariates in the analyses: ethnicity (White, mixed, Asian/Asian British, Black/Black British, others), smoking status (never, previous, current), employment (unemployed, employed), Townsend Deprivation Index (a composite score of employment, car ownership, home ownership and household overcrowding, with higher values indicating a given area's higher

degree of deprivation), statin use (yes/no), hormone replacement therapy (yes/no; women only), alcohol consumption (never, previous, currently <3times/week, currently ≥3times/week), processed/red meat consumption (days/week), resting pulse rate (beats/min), and moderate-to-vigorous physical activity (MVPA) (minutes/day). MVPA time was estimated based on self-reported walking, transportation activities, occupational activities/walking, strenuous/other exercise, and do-it-yourself activities by calibrating them to heart rate and accelerometry data (19) from 12 435 UK adults participating in the Fenland project (20).

**Statistical analyses**

Cox regression models (with age as the underlying time scale) were used to estimate associations of GS and adiposity with all-cause and CVD mortality. First, models were fit to estimate associations between GS and mortality, with adjustment for potential confounders (Model 1). Further adjustments for each of the three adiposity indicators (BMI, WC or %BF) were made in three separate models (Models 2a, 2b and 2c). In parallel with the models using GS as an exposure variable, models using each adiposity measure as an exposure variable were also fitted with adjustment for the same covariates (Model 1) and additional adjustments for GS (Model 2). Models using per-5kg increment in GS as an exposure were fitted by personal/lifestyle risk factor and disease status. GS-mortality associations were stratified by each adiposity variable. Gender- and age-specific quintiles of GS (Q1-Q5) and different adiposity categories were combined to examine joint associations with mortality. All analyses were performed for men and women separately. Subgroup analyses and tests of interaction between GS and age, weight status, waist circumference, %BF, MVPA, TV viewing, smoking, alcohol consumption, hypertension and diabetes were performed. Log-log plots provided support for the proportional hazards assumptions for all covariates. Sensitivity analyses were performed 1) using the maximum GS

from either hand, 2) GS normalized for body weight or fat-free mass to account for variation by body size, 3) excluding the first 2-year mortality follow-up, and 4) excluding individuals who had chronic obstructive pulmonary disease or were 'current'/'previous' smokers at baseline when examining adiposity as exposure (the latter two to minimize the risk of reverse causality). All analyses were performed in STATA/SE Version 14 (StataCorp LP, College Station, TX).

## Results

Of an initial sample of 502,639 participants who undertook baseline data collection, individuals were excluded if they had a history of heart attack, stroke or cancer at baseline (n=55,401) to minimize the risk for reverse causality (8, 21), their censoring date was before the date of baseline data collection (n=3) or they had missing values on any of the variables (n=44,036), leaving 403,199 participants in the final analytic sample (Supplemental Figure 1).

Table 1 shows participants' characteristics across quintiles of GS. The specific cut-points to create the gender- and age-specific quintiles of GS are shown in Supplemental Table 1. A total of 8,081 all-cause deaths occurred during 1,268,314 person-years of follow-up for men and 1,533,538 person-years for women. Differences in BMI, WC, and %BF across quintiles of GS and the correlations between these variables (Supplemental Table 2) were minimal.

Table 2 summarizes associations between GS and all-cause mortality. Compared with the lowest quintile of GS, the highest quintile of GS had considerably lower risks of all-cause mortality in both men and women (except for Q2) after adjusting for confounders (Model 1) plus additional adjustments for each adiposity measure (Model 2): p-values for trends <0.0001. Specifically, hazards of all-cause mortality were approximately 32% (95% confidence interval [CI]: 26%, 38%) and 25% (95%CI: 16%, 33%) lower for men and women in Q5 of GS, respectively, compared with Q1 of GS after adjusting for confounders and BMI (Model 2a). The hazard ratios

(HR) for per-5kg increase in GS was 0.92 for both men (95%CI: 0.90, 0.93) and women (95%CI: 0.89, 0.95) after adjusting for all confounders and BMI (Model 2a). Sensitivity analyses found similar associations with the maximal GS from either hand, and GS unnormalized or normalized for body weight or fat-free mass (Supplemental Figure 2). Another sensitivity analysis removing the first 2 years of follow-up yielded similar results (Supplemental Table 3). The pattern of associations of GS with CVD mortality was similar to the associations with all-cause mortality for men (Table 2). While the HRs were not statistically significant in women, p-values for linear trends were all less than 0.05. The associations of per-5kg increase in GS with all-cause and CVD mortality were significant (p-values<0.05) within almost all of the subgroups examined in both men and women (Figure 1), with some exceptions particularly for women.

Associations of adiposity measures with all-cause and CVD mortality after adjusting for confounders (Model 1) and GS (Model 2) are shown in Supplemental Table 4. There were 'J-shaped' associations between BMI and mortality risk (i.e. substantially lower all-cause mortality only in overweight men compared with normal weight men), which persisted even after excluding individuals who had chronic obstructive pulmonary disease and/or were 'current'/'previous' smokers at baseline (Supplemental Table 5). The highest categories of BMI (i.e. obesity class II) and WC (i.e. abdominal obesity in men) were associated with increased hazards of all-cause and CVD mortality.

Figure 2 shows joint associations of GS quintiles and adiposity categories with all-cause mortality. Compared with normal weight men with the highest level of GS, more obese men with lower GS had higher risks of all-cause mortality. For example, men with the highest level of BMI (i.e. Obesity class II) and lowest level of GS had a 89% higher risk of all-cause mortality (HR: 1.89; 95%CI: 1.50, 2.39) compared with the normal weight men with the highest GS. A

notable observation was the relatively higher mortality risks for normal weight men with lower GS in comparison with more obese men with higher GS. Similar trends of findings were observed with WC and %BF as adiposity indicators.

Similarly, more obese women with lower GS had generally higher all-cause mortality risks compared with normal weight women with higher GS. The HR for women with the highest BMI level (i.e. Obesity class II) and lowest GS was 1.69 (95%CI: 1.32, 2.16) compared with normal weight women with the highest GS. The higher GS quintiles in the Obesity class II category were associated with significantly higher risks of all-cause mortality compared with the reference group. Joint analyses with WC and %BF as adiposity indicators found more obese women with higher GS to have lower all-cause mortality risks compared with non-obese women with lower GS. This pattern of associations was, in general, similar to the associations observed for CVD mortality (Figure 3).

The lower GS quintiles had relatively higher all-cause (Supplemental Figure 3) and CVD mortality (Supplemental Figure 4) risks compared with the highest GS quintile within each adiposity stratum in both men and women.

## Discussion

This study investigated the complex interplay of GS and various clinical adiposity measures with mortality from all causes and CVD in middle-aged and older men and women. Overall, greater GS was strongly associated with lower all-cause mortality risks, independently of adiposity measures. Moreover, every 5kg increment in GS was associated with about 8% lower hazard of mortality across nearly all subgroups defined by demographic and lifestyle risk factors or disease status. In contrast, adiposity measures had non-significant and/or inconsistent associations with mortality, although obesity class II and abdominal obesity were strong predictors of mortality,

independent of GS. The mortality risk was highest for men and women with the lowest level of GS and the highest level of adiposity in the combined analyses. More importantly, obese individuals with greater GS had lower or similar mortality risks compared with non-obese individuals with lower GS. The pattern of associations between GS and CVD mortality was comparable to the findings for all-cause mortality. Overall, our findings provide compelling rationales for developing interventions and policies to improve muscular strength and reduce excess adiposity to minimize mortality risk.

The findings of this study are consistent with previous research by Leong at al. (9), which also demonstrated the high prognostic value of GS for various mortality and adverse health outcomes in 139,691 adults from 17 countries of different economic status. The HR of all-cause mortality for every 5kg reduction was 1.16 in Leong et al. study (9) but 1.08 (i.e. 1/0.92) in the present study. Some potential reasons for the difference are the use of gender- and age-specific quintiles of GS to take into account the inherent variation of GS by gender and age since GS is higher in men and younger individuals, and the exclusion of baseline medical conditions to minimize potential bias due to underlying subclinical conditions on GS and mortality in the present study. Furthermore, the use of a substantially larger sample allowed for comprehensive subgroup analyses by a number of lifestyle risk factors as well as disease status.

The present study is generally consistent with the previous studies (11-14) in terms of the independent and joint associations of GS and adiposity with mortality outcomes. For instance, greater muscle strength predicted mortality independent of adiposity (11-14). In addition, the highest mortality risk was observed in individuals with the lowest muscle strength level and the highest adiposity level, implying the interactive impacts of muscle strength and adiposity on mortality (11, 12, 14). However, a novel observation of the present study is that strong obese

individuals had relatively lower mortality risks compared with weak non-obese individuals. This suggests that improving muscle strength may be a more important public health priority than reducing adiposity levels in decreasing mortality risks, although excessive adiposity itself is a strong risk factor for mortality (15). Another novel aspect of this study over the previous studies (11-14) is the use of a large cohort dataset, which enabled to create multiple sub-groups of GS and various clinical adiposity indicators in examining the joint associations with mortality in men and women separately.

The present study found that men had more consistent associations between GS and mortality (independent of adiposity) than women, which is in line with previous research (13). There is also evidence on the weaker associations of GS with all-cause mortality for women (22). In this regard, convincing evidence suggests an age-related decline in muscle strength in women (particularly after menopause) can be prevented through estrogen-hormone replacement therapy (23). However, none of the previous studies (13, 22) included estrogen-hormone replacement therapy as a potential confounder in the models for women whereas the present study did. Our study clearly demonstrated lower mortality rates for both men and women with greater GS. Moreover, given that current public health guidelines (24) recommend that both men and women do muscle-strengthening activities at least twice a week, interventions and policies should be designed and implemented in a way to encourage both genders to engage in regular muscle-strengthening activities, regardless of their adiposity levels.

Compelling evidence suggests that resistance exercise can result in improvements in muscle strength (including GS) and neuromotor functions in healthy and clinical adult populations (25). It appears that muscle strength gained through resistance exercise can diminish rapidly after the termination of training, but its effects on neuromotor functions can be sustained for a relatively

long period of time even with a weekly session of moderate-to-vigorous intensity resistance exercise (25). We observed weak relationships between GS and adiposity measures, suggesting greater GS is determined based on better neuromotor functions rather than higher adiposity itself. Nonetheless, it is important to point out that the effects of resistance training are typically site-specific (26), so training solely GS may not necessarily yield favorable effects on other parts of the body. Thus, efforts should be placed on improving whole-body muscle strength as well as neuromuscular functions.

Effects of resistance training on reducing metabolic risk are also well-documented. Specifically, glucose metabolisms and insulin sensitivity can be enhanced in response to resistance exercise (27). In the present study, the prevalence of diabetes was lower in both men and women across incremental GS quintiles. It may be that participation in resistance training was higher in those with greater GS since people use their hands in most upper-body resistance training. This suggests individuals with greater muscle strength may sustain metabolically healthier lives. Furthermore, a meta-analysis of randomized-controlled trials concluded that resistance training programs reduced levels of lipids and lipoproteins circulating in the blood stream (28). However, high-intensity resistance training may increase arterial stiffness (29), which may then increase the risk of mortality and CVD (30). More evidence is needed to determine the specific dose-response relationship between resistance training and health outcomes.

This study is not without limitations. First, the use of data from an observational prospective study cannot fully determine causal relationships between GS and mortality. However, we excluded individuals with critical medical conditions at baseline in the primary analysis, and further excluded individuals who died in the first 2 years of follow-up and individuals who had respiratory disease or were current or previous smokers at baseline in the sensitivity analysis, in

order to minimize the risk for reverse causality. Second, due to the lack of sampling strategies for recruiting samples in UK Biobank, results of this study may only be generalizable to those of similar characteristics to the sample analyzed here. Another limitation is the measurement method for aerobic fitness, a strong mortality predictor (31). Ideally, this is measured as oxygen consumption during maximal exercise tests. We adjusted for resting pulse rate instead, which is strongly associated with maximal oxygen consumption (32). The relatively low number of death cases in the analysis for CVD mortality is another limitation. Finally, the use of self-reported data for some of the covariates may have increased the risk of residual confounding.

## Conclusions

Men and women with greater GS had lower risks of all-cause and CVD mortality, independent of adiposity. While excess adiposity *per se* presents substantial risk of mortality, the risk associated with excess adiposity was reduced, although not completely eliminated, through greater GS. Public health efforts should aim to improve muscle strength of the population in all adiposity levels.

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The authors have no conflict of interest. YK designed this study, performed statistical analysis, and drafted an initial version of the manuscript. KW, DCL, SJS, NW, and SB all contributed to conceptualizing the study idea and developing the analytical plans, and provided assistance with statistical analysis. All authors critically reviewed, approved of the final version of the manuscript, and agreed to be responsible for all facets of this work.

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Table 1. Participants' characteristics

| | Men (n=183,006) | | | | | | Women (n=220,193) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | All | Quintiles of grip strength | | | | | All | Quintiles of grip strength | | | | |
| Variables | | Q1 | Q2 | Q3 | Q4 | Q5 | | Q1 | Q2 | Q3 | Q4 | Q5 |
| Grip strength, kg | 39.7 (8.8) | 27.7 (4.9) | 35.3 (26) | 39.3 (2.7) | 43.6 (2.9) | 51.2 (4.9) | 23.5 (6.2) | 14.7 (3.6) | 20.2 (2.1) | 22.9 (2.1) | 26.2 (2.1) | 31.2 (3.5) |
| Age, years | 56.2 (8.2) | 56.4 (8.4) | 55.8 (8.3) | 56.5 (8.1) | 56.5 (8.2) | 55.6 (8.1) | 56.0 (8.0) | 56.7 (8.0) | 55.8 (8.2) | 56.5 (8.0) | 55.7 (7.7) | 55.4 (8.1) |
| Ethnicity, % | | | | | | | | | | | | |
| White | 94.4% | 89.6% | 93.7% | 95.5% | 96.3% | 96.6% | 94.4% | 90.9% | 94.0% | 95.1% | 95.9% | 95.6% |
| Mixed | 0.5% | 0.5% | 0.6% | 0.5% | 0.5% | 0.5% | 0.7% | 0.7% | 0.7% | 0.6% | 0.7% | 0.8% |
| Asian/Asian British | 2.6% | 6.3% | 3.2% | 2.0% | 1.2% | 0.7% | 2.1% | 5.0% | 2.5% | 1.7% | 1.2% | 0.6% |
| Black/Black British | 1.6% | 2.0% | 1.5% | 1.4% | 1.4% | 1.7% | 1.8% | 1.8% | 1.6% | 1.7% | 1.5% | 2.4% |
| Others | 0.9% | 1.6% | 1.0% | 0.7% | 0.7% | 0.5% | 1.0% | 1.6% | 1.1% | 0.9% | 0.8% | 0.6% |
| Smoking status, % | | | | | | | | | | | | |
| Never | 50.4% | 51.4% | 50.9% | 50.7% | 49.6% | 49.7% | 60.3% | 61.6% | 61.4% | 60.5% | 59.6% | 58.8% |
| Previous | 37.3% | 35.0% | 36.5% | 37.1% | 38.7% | 38.9% | 31.0% | 29.2% | 29.9% | 31.3% | 31.7% | 32.5% |
| Current | 12.3% | 13.6% | 12.6% | 12.1% | 11.7% | 11.4% | 8.7% | 9.2% | 8.7% | 8.2% | 8.7% | 8.7% |
| Employment, % | | | | | | | | | | | | |
| Unemployed | 35.9% | 42.2% | 35.3% | 36.0% | 35.6% | 30.9% | 43.0% | 50.2% | 42.4% | 44.4% | 39.3% | 39.9% |
| Townsend deprivation index | -1.33 (3.1) | -0.58 (3.4) | -1.16 (3.1) | -1.44 (3.0) | -1.62 (2.9) | -1.79 (2.8) | -1.39 (3.0) | -0.95 (3.2) | -1.28 (3.0) | -1.47 (3.0) | -1.57 (2.9) | -1.59 (2.9) |
| Statin use, % | 19.7% | 23.6% | 19.7% | 19.8% | 18.9% | 16.8% | 11.7% | 15.4% | 12.1% | 11.5% | 10.3% | 10.0% |
| Hormone replacement therapy (W), % | (N/A) | (N/A) | (N/A) | (N/A) | (N/A) | (N/A) | 7.5% | 7.4% | 7.2% | 7.2% | 7.7% | 7.9% |
| Alcohol Consumption, % | | | | | | | | | | | | |
| Never | 2.7% | 4.7% | 2.8% | 2.4% | 1.9% | 1.6% | 5.6% | 9.1% | 6.1% | 5.1% | 4.4% | 4.1% |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Previous | 3.3% | 5.0% | 3.4% | 2.9% | 2.7% | 2.3% | 3.4% | 4.8% | 3.7% | 3.2% | 2.9% | 2.7% |
| Current (<3times/week) | 41.8% | 44.3% | 42.7% | 41.3% | 40.3% | 40.7% | 53.7% | 56.4% | 55.1% | 53.4% | 52.9% | 51.5% |
| Current (≥3times/week) | 52.3% | 45.9% | 51.0% | 53.5% | 55.1% | 55.3% | 37.2% | 29.8% | 35.2% | 38.2% | 39.7% | 41.7% |
| Processed/red meat consumption, days/week | 1.04 (0.60) | 1.05 (0.64) | 1.04 (0.61) | 1.04 (0.59) | 1.03 (0.58) | 1.05 (0.58) | 0.78 (0.50) | 0.79 (0.53) | 0.78 (0.50) | 0.78 (0.50) | 0.78 (0.49) | 0.78 (0.49) |
| Resting pulse rate, beats/min | 68.3 (11.7) | 69.5 (12.3) | 68.4 (11.8) | 68.0 (11.6) | 67.9 (11.6) | 67.9 (11.5) | 70.1 (10.5) | 70.8 (10.7) | 70.1 (10.5) | 69.9 (10.4) | 69.8 (10.4) | 69.9 (10.6) |
| Self-reported MVPA time, min/day | 82.3 (22.9) | 78.4 (20.7) | 81.8 (22.2) | 82.4 (24.0) | 83.1 (23.0) | 85.3 (23.6) | 51.6 (19.5) | 49.2 (16.1) | 51.0 (18.8) | 51.3 (18.8) | 52.5 (19.5) | 53.5 (22.9) |
| BMI, kg/m$^2$ | 27.7 (4.2) | 27.7 (4.6) | 27.6 (4.3) | 27.6 (4.1) | 27.7 (3.9) | 28.2 (3.9) | 27.0 (5.1) | 27.6 (5.5) | 26.9 (5.1) | 26.8 (5.0) | 26.8 (4.9) | 27.0 (5.0) |
| Normal weight, % | 25.0% | 28.0% | 27.8% | 25.9% | 24.3% | 19.6% | 39.2% | 35.0% | 39.9% | 40.6% | 41.0% | 39.1% |
| Overweight, % | 50.1% | 46.2% | 48.6% | 50.6% | 51.7% | 52.9% | 37.3% | 37.0% | 37.0% | 37.3% | 37.5% | 37.7% |
| Obesity class I, % | 19.4% | 19.1% | 18.0% | 18.5% | 19.3% | 22.0% | 15.8% | 17.9% | 15.7% | 15.2% | 14.8% | 15.5% |
| Obesity class II, % | 5.5% | 6.7% | 5.6% | 5.0% | 4.7% | 5.5% | 7.7% | 10.1% | 7.4% | 6.9% | 6.7% | 7.6% |
| WC, cm | 96.6 (11.1) | 97.0 (12.0) | 96.2 (11.4) | 96.2 (11.0) | 96.4 (10.7) | 97.3 (10.5) | 84.5 (12.4) | 86.0 (13.1) | 84.2 (12.3) | 83.9 (12.1) | 83.8 (12.1) | 84.6 (12.2) |
| <94cm(M); <80cm(W) | 45.3% | 44.8% | 47.5% | 46.6% | 46.0% | 41.8% | 42.5% | 37.9% | 43.2% | 44.1% | 44.4% | 42.1% |
| 94-102cm(M); 80-88cm(W) | 25.4% | 23.7% | 24.5% | 25.4% | 25.7% | 27.2% | 21.9% | 21.3% | 21.8% | 21.9% | 22.1% | 22.3% |
| ≥102cm(M); ≥88cm(W) | 29.4% | 31.5% | 28.1% | 28.0% | 28.3% | 30.9% | 35.6% | 40.8% | 34.9% | 34.0% | 33.5% | 35.6% |
| %BF | 25.1 (5.8) | 25.8 (6.1) | 25.2 (5.9) | 25.0 (5.7) | 24.8 (5.6) | 24.7 (5.5) | 36.4 (6.9) | 37.5 (7.0) | 36.5 (6.9) | 36.4 (6.8) | 36.1 (6.8) | 36.0 (6.9) |
| ≤20%(M); ≤30%(W) | 18.3% | 16.5% | 18.2% | 18.8% | 19.1% | 18.9% | 17.6% | 14.4% | 17.2% | 17.5% | 18.7% | 19.5% |
| 20-25%(M); 30-33%(W) | 30.9% | 27.5% | 30.3% | 31.0% | 32.1% | 33.1% | 12.8% | 11.2% | 13.0% | 12.8% | 13.5% | 13.4% |
| >25%(M); >33%(W) | 50.8% | 56.0% | 51.5% | 50.2% | 48.8% | 47.9% | 69.6% | 74.4% | 69.8% | 69.7% | 67.8% | 67.1% |
| Fat free mass, kg | 63.8 (7.8) | 61.0 (8.0) | 62.3 (7.5) | 63.3 (7.3) | 64.5 (7.1) | 67.3 (7.4) | 44.5 (5.0) | 43.4 (5.2) | 43.7 (4.8) | 44.0 (4.7) | 44.8 (4.7) | 46.3 (4.9) |
| Systolic blood pressure, mm Hg | 140.9 (17.3) | 139.2 (17.7) | 139.8 (17.2) | 141.1 (17.4) | 142.0 (17.2) | 142.3 (16.9) | 135.0 (19.2) | 134.3 (19.2) | 133.8 (19.2) | 135.2 (19.3) | 135.1 (19.0) | 136.1(19.1) |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Diastolic blood pressure, mm Hg | 84.3 (9.9) | 83.2 (10.1) | 83.8 (10.0) | 84.3 (9.9) | 84.8 (9.9) | 85.4 (9.8) | 80.7 (10.0) | 80.2 (10.0) | 80.1 (10.0) | 80.5 (9.9) | 80.8 (9.9) | 81.5 (9.9) |
| Hypertension, % | 61.1% | 60.3% | 58.7% | 60.9% | 62.4% | 62.8% | 47.7% | 49.3% | 46.0% | 47.9% | 46.8% | 48.6% |
| Diabetes, % | 6.1% | 9.7% | 6.5% | 5.8% | 4.9% | 4.1% | 3.4% | 5.4% | 3.6% | 3.1% | 2.8% | 2.6% |

Note: The quintiles of grip strength were gender- and age-specific. Body Mass Index (BMI) was used to categorize participants into normal weight ($18.5kg/m^2 \leq BMI < 25kg/m^2$), overweight ($25kg/m^2 \leq BMI < 30kg/m^2$), obesity class I ($30kg/m^2 \leq BMI < 35kg/m^2$) and obesity class II ($BMI \geq 35kg/m^2$). Hypertension was defined as systolic/diastolic blood pressure ≥140/90mm Hg, reported physician diagnosis of hypertension, or reported medication use to regulate blood pressure. Participants were considered to have diabetes if they reported a physician diagnosis of diabetes, or taking glucose-lowering treatment.

Table 2. Independent associations of grip strength with all-cause and cardiovascular disease (CVD) mortality.

| | | | | | | Hazard ratios (95% confidence interval) for mortality | | | |
|---|---|---|---|---|---|---|---|---|---|
| Mortality outcome | Gender | Comparisons | Number of deaths | Person-years of follow-up | Mortality rate | Model 1 | Model 2a | Model 2b | Model 2c |
| **All-cause** | Men | | 5,049 | 1,268,314 | 398.1 | | | | |
| | | Quintiles of grip strength | | | | | | | |
| | | Q1 (Reference) | 1,389 | 241,358 | 575.5 | 1.00 (Reference) | 1.00 (Reference) | 1.00 (Reference) | 1.00 (Reference) |
| | | Q2 | 933 | 232,139 | 401.9 | 0.80 (0.73, 0.87) | 0.81 (0.75, 0.88) | 0.80 (0.73, 0.87) | 0.80 (0.73, 0.87) |
| | | Q3 | 920 | 253,118 | 363.5 | 0.71 (0.65, 0.77) | 0.72 (0.66, 0.78) | 0.70 (0.65, 0.77) | 0.71 (0.65, 0.77) |
| | | Q4 | 972 | 268,240 | 362.4 | 0.72 (0.66, 0.78) | 0.73 (0.67, 0.79) | 0.72 (0.66, 0.78) | 0.72 (0.66, 0.78) |
| | | Q5 | 835 | 273,460 | 305.3 | 0.67 (0.62, 0.73) | 0.68 (0.62, 0.74) | 0.67 (0.61, 0.73) | 0.67 (0.62, 0.74) |
| | | *P for linear trend* | | | | <0.0001 | <0.0001 | <0.0001 | <0.0001 |
| | | Per 5kg increment in grip strength | | | | 0.91 (0.90, 0.93) | 0.92 (0.90, 0.93) | 0.91 (0.90, 0.93) | 0.91 (0.90, 0.93) |
| | Women | | 3,238 | 1,533,538 | 211.1 | | | | |
| | | Quintiles of grip strength | | | | | | | |
| | | Q1 (Reference) | 746 | 270,638 | 275.6 | 1.00 (Reference) | 1.00 (Reference) | 1.00 (Reference) | 1.00 (Reference) |
| | | Q2 | 652 | 274,981 | 237.1 | 0.96 (0.86, 1.06) | 0.97 (0.87, 1.08) | 0.97 (0.87, 1.07) | 0.96 (0.86, 1.06) |
| | | Q3 | 656 | 316,838 | 207.0 | 0.81 (0.73, 0.90) | 0.82 (0.74, 0.91) | 0.82 (0.74, 0.91) | 0.81 (0.73, 0.90) |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | Q4 | 592 | 323,506 | 182.0 | 0.79 (0.71, 0.88) | 0.80 (0.72, 0.89) | 0.80 (0.71, 0.89) | 0.79 (0.71, 0.88) |
| | | Q5 | 592 | 347,576 | 170.3 | 0.74 (0.67, 0.83) | 0.75 (0.67, 0.84) | 0.74 (0.67, 0.83) | 0.74 (0.67, 0.83) |
| | | *P for linear trend* | | | | <0.0001 | <0.0001 | <0.0001 | <.0001 |
| | | Per 5kg increment in grip strength | | | | 0.91 (0.89, 0.94) | 0.92 (0.89, 0.95) | 0.91 (0.89, 0.94) | 0.91 (0.89, 0.94) |
| **CVD** | Men | | 1,256 | 1,268,314 | 99.0 | | | | |
| | | Quintiles of grip strength | | | | | | | |
| | | Q1 (Reference) | 373 | 241,358 | 154.5 | 1.00 (Reference) | 1.00 (Reference) | 1.00 (Reference) | 1.00 (Reference) |
| | | Q2 | 246 | 232,139 | 106.0 | 0.81 (0.69, 0.96) | 0.82 (0.70, 0.97) | 0.81 (0.69, 0.95) | 0.81 (0.69, 0.96) |
| | | Q3 | 222 | 253,118 | 87.7 | 0.66 (0.56, 0.78) | 0.67 (0.56, 0.79) | 0.67 (0.56, 0.79) | 0.67 (0.57, 0.79) |
| | | Q4 | 235 | 268,240 | 87.6 | 0.68 (0.58, 0.81) | 0.69 (0.58, 0.81) | 0.68 (0.58, 0.81) | 0.69 (0.58, 0.82) |
| | | Q5 | 180 | 273,460 | 65.8 | 0.58 (0.48, 0.69) | 0.57 (0.47, 0.68) | 0.57 (0.47, 0.68) | 0.58 (0.48, 0.70) |
| | | *P for linear trend* | | | | <0.0001 | <0.0001 | <0.0001 | <0.0001 |
| | | Per 5kg increment in grip strength | | | | 0.88 (0.84, 0.91) | 0.88 (0.85, 0.91) | 0.88 (0.85, 0.91) | 0.88 (0.86, 0.92) |
| | Women | | 485 | 1,533,538 | 31.6 | | | | |
| | | Quintiles of grip strength | | | | | | | |
| | | Q1 (Reference) | 122 | 270,638 | 45.1 | 1.00 (Reference) | 1.00 (Reference) | 1.00 (Reference) | 1.00 (Reference) |
| | | Q2 | 98 | 274,981 | 35.6 | 0.93 (0.72, 1.22) | 0.93 (0.71, 1.21) | 0.95 (0.73, 1.24) | 0.94 (0.72, 1.23) |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Q3 | 89 | 316,838 | 28.1 | 0.73 (0.56, 0.97) | 0.72 (0.55, 0.95) | 0.75 (0.57, 0.99) | 0.74 (0.56, 0.97) |
| Q4 | 92 | 323,506 | 28.4 | 0.85 (0.65, 1.12) | 0.83 (0.63, 1.10) | 0.86 (0.65, 1.13) | 0.85 (0.65, 1.12) |
| Q5 | 84 | 347,576 | 24.2 | 0.74 (0.56, 0.98) | 0.73 (0.55, 0.97) | 0.74 (0.56, 0.98) | 0.74 (0.56, 0.98) |
| *P for linear trend* | | | | 0.028 | 0.021 | 0.021 | 0.027 |
| Per 5kg increment in grip strength | | | | 0.93 (0.87, 0.99) | 0.93 (0.86, 1.01) | 0.94 (0.87, 1.01) | 0.94 (0.87, 1.01) |

Note: All Cox regression models used age as the underlying time variable. The quintiles of grip strength were gender- and age-specific. Mortality rate is crude mortality rate per 100,000-person years

Model 1: Adjusted for ethnicity (White, mixed, Asian/Asian British, Black/Black British, others), smoking status (never, previous, current), employment (unemployed, employed), Townsend Deprivation Index, statin use (yes/no), hormone replacement therapy (yes/no; women only), alcohol consumption (never, previous, currently <3times/week, currently ≥3times/week), processed/red meat consumption (days/week), resting pulse rate (beats/min), and moderate-to-vigorous physical activity time (minutes/day).

Model 2a: Adjusted for all confounders included in Model 1 plus body mass index. Cases with BMI<18.5 (n=369 for men; n=1,525 for women) were excluded.

Model 2b: Adjusted for all confounders included in Model 1 plus waist circumference.

Model 2c: Adjusted for all confounders included in Model 1 plus percent body fat.

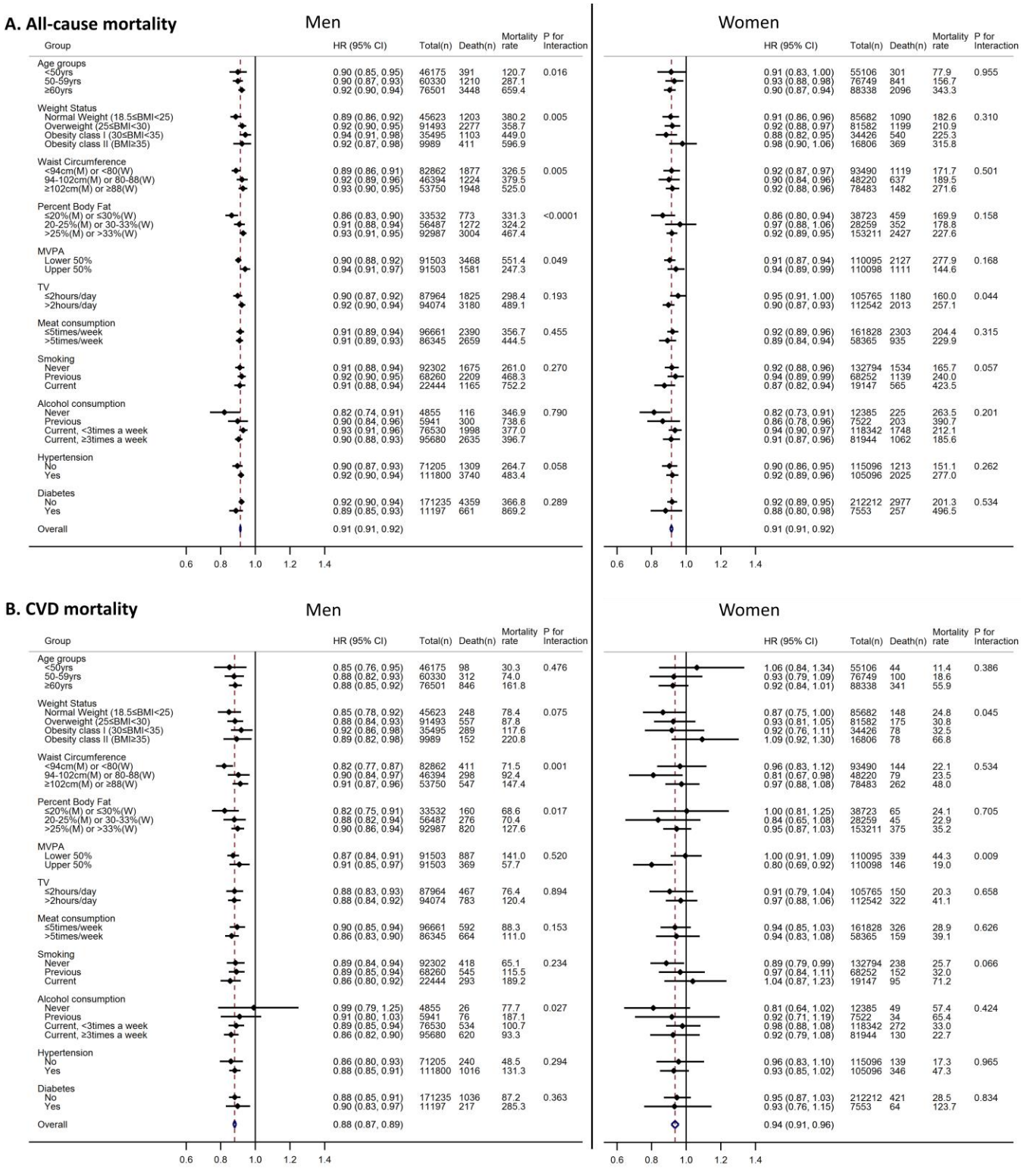
## Figure Legends

Figure 1. Associations of per-5kg increment of grip strength with all-cause and cardiovascular disease (CVD) mortality for men and women. Models (using age as the underlying time variable) were adjusted for ethnicity (White, mixed, Asian/Asian British, Black/Black British, others), smoking status (never, previous, current; except for models stratified by smoking status), employment (unemployed, employed), Townsend Deprivation Index, statin use (yes/no), hormone replacement therapy (yes/no; women only), alcohol consumption (never, previous, currently <3times/week, currently ≥3times/week; except for models stratified by alcohol consumption), processed/red meat consumption (days/week; except for models stratified by processed/red meat consumption), resting pulse rate (beats/min), moderate-to-vigorous physical activity (MVPA) time (minutes/day; except for models stratified by MVPA), and body mass index (BMI) (except for models stratified by BMI, waist circumference and percent body fat). Hypertension was defined as systolic/diastolic blood pressure ≥140/90mm Hg, reported physician diagnosis of hypertension, or reported medication use to regulate blood pressure. Participants were considered to have diabetes if they reported a physician diagnosis of diabetes, or taking glucose-lowering treatment. Mortality rate is crude mortality rate per 100,000-person years. Cases with BMI<18.5 (n=369 for men; n=1,525 for women) were excluded in the BMI-stratified models. Abbreviations: HR – hazard ratio; CI – confidence interval; M – men; W– Women.

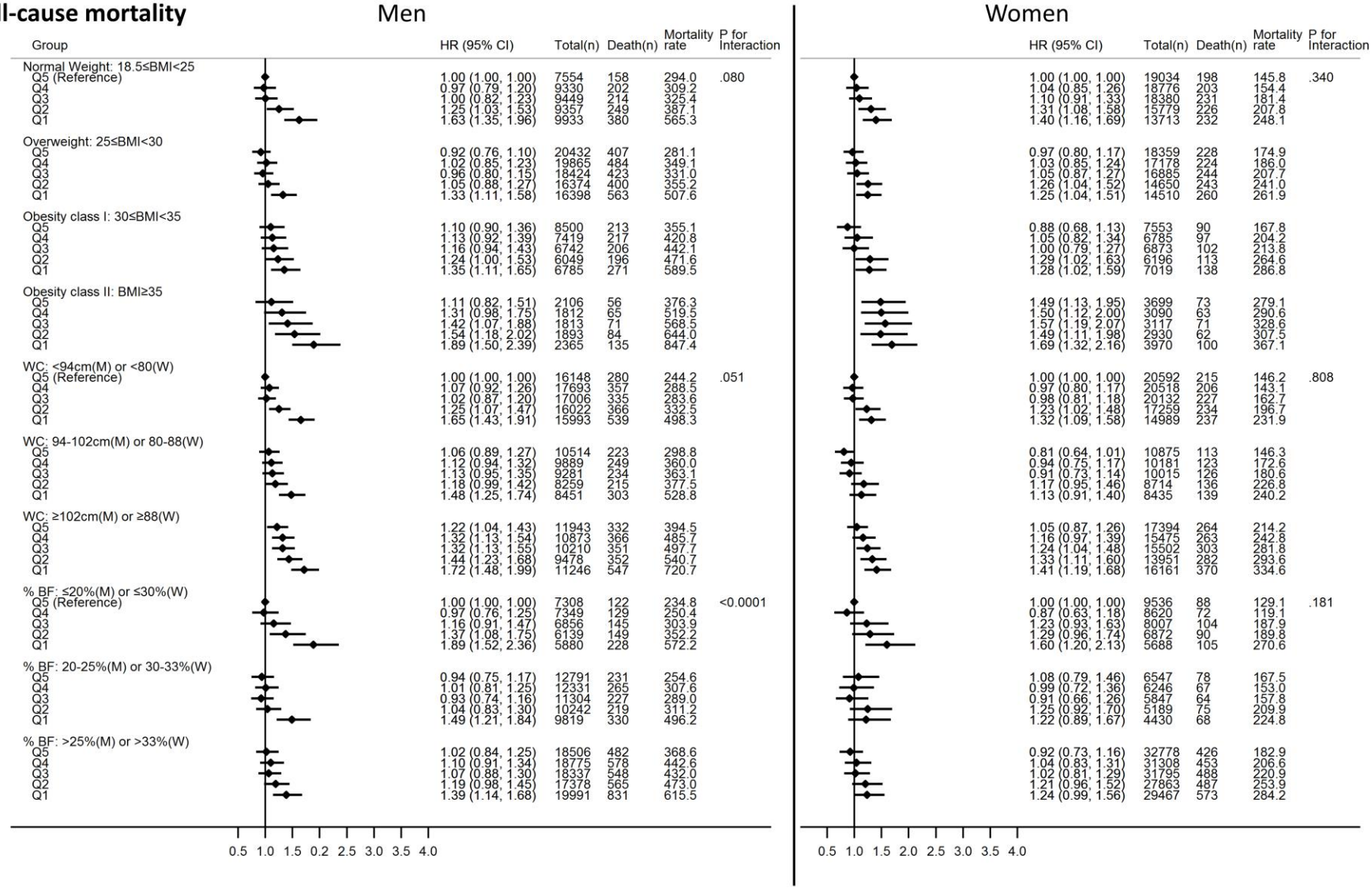
Figure 2. Joint associations of grip strength and body mass index, waist circumference or percent body fat with all-cause mortality for men and women. All Cox regression models (using age as the underlying time variable) were adjusted for ethnicity (White, mixed, Asian/Asian British, Black/Black British, others), smoking status (never, previous, current), employment

(unemployed, employed), Townsend Deprivation Index, statin use (yes/no), hormone replacement therapy (yes/no; women only), alcohol consumption (never, previous, currently <3times/week, currently ≥3times/week), processed/red meat consumption (days/week), resting pulse rate (beats/min), and moderate-to-vigorous physical activity time (minutes/day). The quintiles of grip strength were gender- and age-specific. Mortality rate is crude mortality rate per 100,000-person years. Cases with BMI<18.5 (n=369 for men; n=1,525 for women) were excluded in the models with BMI. Abbreviations: HR – hazard ratio; CI – confidence interval; M – men; W– Women.

Figure 3. Joint associations of grip strength and body mass index, waist circumference or percent body fat with cardiovascular disease (CVD) mortality for men and women. All Cox regression models (using age as the underlying time variable) were adjusted for ethnicity (White, mixed, Asian/Asian British, Black/Black British, others), smoking status (never, previous, current), employment (unemployed, employed), Townsend Deprivation Index, statin use (yes/no), hormone replacement therapy (yes/no; women only), alcohol consumption (never, previous, currently <3times/week, currently ≥3times/week), processed/red meat consumption (days/week), resting pulse rate (beats/min), and moderate-to-vigorous physical activity time (minutes/day). The quintiles of grip strength were gender- and age-specific. Mortality rate is crude mortality rate per 100,000-person years. Cases with BMI<18.5 (n=369 for men; n=1,525 for women) were excluded in the models with BMI. Abbreviations: HR – hazard ratio; CI – confidence interval; M – men; W– Women.


A. All-cause mortality
Men
Women
Group
HR (95% CI)
Total(n)
Death(n)
Mortality rate
P for Interaction
Age groups
<50yrs 0.90 (0.85, 0.95) 46175 391 120.7 0.016
50-59yrs 0.90 (0.87, 0.93) 60330 1210 287.1
≥60yrs 0.92 (0.90, 0.94) 76501 3448 659.4
Weight Status
Normal Weight (18.5≤BMI<25) 0.89 (0.86, 0.92) 45623 1203 380.2 0.005
Overweight (25≤BMI<30) 0.92 (0.90, 0.95) 91493 2277 358.7
Obesity class I (30≤BMI<35) 0.94 (0.91, 0.98) 35495 1103 449.0
Obesity class II (BMI≥35) 0.92 (0.87, 0.98) 9989 411 596.9
Waist Circumference
<94cm(M) or <80(W) 0.89 (0.86, 0.91) 82862 1877 326.5 0.005
94-102cm(M) or 80-88(W) 0.92 (0.89, 0.96) 46394 1224 379.5
≥102cm(M) or ≥88(W) 0.93 (0.90, 0.95) 53750 1948 525.0
Percent Body Fat
≤20%(M) or ≤30%(W) 0.86 (0.83, 0.90) 33532 773 331.3 <0.0001
20-25%(M) or 30-33%(W) 0.91 (0.88, 0.94) 56487 1272 324.2
>25%(M) or >33%(W) 0.93 (0.91, 0.95) 92987 3004 467.4
MVPA
Lower 50% 0.90 (0.88, 0.92) 91503 3468 551.4 0.049
Upper 50% 0.94 (0.91, 0.97) 91503 1581 247.3
TV
≤2hours/day 0.90 (0.87, 0.92) 87964 1825 298.4 0.193
>2hours/day 0.92 (0.90, 0.94) 94074 3180 489.1
Meat consumption
≤5times/week 0.91 (0.89, 0.94) 96661 2390 356.7 0.455
>5times/week 0.91 (0.89, 0.93) 86345 2659 444.5
Smoking
Never 0.91 (0.88, 0.94) 92302 1675 261.0 0.270
Previous 0.92 (0.90, 0.95) 68260 2209 468.3
Current 0.91 (0.88, 0.94) 22444 1165 752.2
Alcohol consumption
Never 0.82 (0.74, 0.91) 4855 116 346.9 0.790
Previous 0.90 (0.84, 0.96) 5941 300 738.6
Current, <3times a week 0.93 (0.91, 0.96) 76530 1998 377.0
Current, ≥3times a week 0.90 (0.88, 0.93) 95680 2635 396.7
Hypertension
No 0.90 (0.87, 0.93) 71205 1309 264.7 0.058
Yes 0.92 (0.90, 0.94) 111800 3740 483.4
Diabetes
No 0.92 (0.90, 0.94) 171235 4359 366.8 0.289
Yes 0.89 (0.85, 0.93) 11197 661 869.2
Overall 0.91 (0.91, 0.92)
0.6 0.8 1.0 1.2 1.4
0.91 (0.83, 1.00) 55106 301 77.9 0.955
0.93 (0.88, 0.98) 76749 841 156.7
0.90 (0.87, 0.94) 88338 2096 343.3
0.91 (0.86, 0.96) 85682 1090 182.6 0.310
0.92 (0.88, 0.97) 81582 1199 210.9
0.88 (0.82, 0.95) 34426 540 225.3
0.98 (0.90, 1.06) 16806 369 315.8
0.92 (0.87, 0.97) 93490 1119 171.7 0.501
0.90 (0.84, 0.96) 48220 637 189.5
0.92 (0.88, 0.96) 78483 1482 271.6
0.86 (0.80, 0.94) 38723 459 169.9 0.158
0.97 (0.88, 1.06) 28259 352 178.8
0.92 (0.89, 0.95) 153211 2427 227.6
0.91 (0.87, 0.94) 110095 2127 277.9 0.168
0.94 (0.89, 0.99) 110098 1111 144.6
0.95 (0.91, 1.00) 105765 1180 160.0 0.044
0.90 (0.87, 0.93) 112542 2013 257.1
0.92 (0.89, 0.96) 161828 2303 204.4 0.315
0.89 (0.84, 0.94) 58365 935 229.9
0.92 (0.88, 0.96) 132794 1534 165.7 0.057
0.94 (0.89, 0.99) 68252 1139 240.0
0.87 (0.82, 0.94) 19147 565 423.5
0.82 (0.73, 0.91) 12385 225 263.5 0.201
0.86 (0.78, 0.96) 7522 203 390.7
0.94 (0.90, 0.97) 118342 1748 212.1
0.91 (0.87, 0.96) 81944 1062 185.6
0.90 (0.86, 0.95) 115096 1213 151.1 0.262
0.92 (0.89, 0.96) 105096 2025 277.0
0.92 (0.89, 0.95) 212212 2977 201.3 0.534
0.88 (0.80, 0.98) 7553 257 496.5
0.91 (0.91, 0.92)
0.6 0.8 1.0 1.2 1.4
B. CVD mortality
Men
Women
Group
HR (95% CI)
Total(n)
Death(n)
Mortality rate
P for Interaction
Age groups
<50yrs 0.85 (0.76, 0.95) 46175 98 30.3 0.476
50-59yrs 0.88 (0.82, 0.93) 60330 312 74.0
≥60yrs 0.88 (0.85, 0.92) 76501 846 161.8
Weight Status
Normal Weight (18.5≤BMI<25) 0.85 (0.78, 0.92) 45623 248 78.4 0.075
Overweight (25≤BMI<30) 0.88 (0.84, 0.93) 91493 557 87.8
Obesity class I (30≤BMI<35) 0.92 (0.86, 0.98) 35495 289 117.6
Obesity class II (BMI≥35) 0.89 (0.82, 0.98) 9989 152 220.8
Waist Circumference
<94cm(M) or <80(W) 0.82 (0.77, 0.87) 82862 411 71.5 0.001
94-102cm(M) or 80-88(W) 0.90 (0.84, 0.97) 46394 298 92.4
≥102cm(M) or ≥88(W) 0.91 (0.87, 0.96) 53750 547 147.4
Percent Body Fat
≤20%(M) or ≤30%(W) 0.82 (0.75, 0.91) 33532 160 68.6 0.017
20-25%(M) or 30-33%(W) 0.88 (0.82, 0.94) 56487 276 70.4
>25%(M) or >33%(W) 0.90 (0.86, 0.94) 92987 820 127.6
MVPA
Lower 50% 0.87 (0.84, 0.91) 91503 887 141.0 0.520
Upper 50% 0.91 (0.85, 0.97) 91503 369 57.7
TV
≤2hours/day 0.88 (0.83, 0.93) 87964 467 76.4 0.894
>2hours/day 0.88 (0.84, 0.92) 94074 783 120.4
Meat consumption
≤5times/week 0.90 (0.85, 0.94) 96661 592 88.3 0.153
>5times/week 0.86 (0.83, 0.90) 86345 664 111.0
Smoking
Never 0.89 (0.84, 0.94) 92302 418 65.1 0.234
Previous 0.89 (0.85, 0.94) 68260 545 115.5
Current 0.86 (0.80, 0.92) 22444 293 189.2
Alcohol consumption
Never 0.99 (0.79, 1.25) 4855 26 77.7 0.027
Previous 0.91 (0.80, 1.03) 5941 76 187.1
Current, <3times a week 0.89 (0.85, 0.94) 76530 534 100.7
Current, ≥3times a week 0.86 (0.82, 0.90) 95680 620 93.3
Hypertension
No 0.86 (0.80, 0.93) 71205 240 48.5 0.294
Yes 0.88 (0.85, 0.91) 111800 1016 131.3
Diabetes
No 0.88 (0.85, 0.91) 171235 1036 87.2 0.363
Yes 0.90 (0.83, 0.97) 11197 217 285.3
Overall 0.88 (0.87, 0.89)
0.6 0.8 1.0 1.2 1.4
1.06 (0.84, 1.34) 55106 44 11.4 0.386
0.93 (0.79, 1.09) 76749 100 18.6
0.92 (0.84, 1.01) 88338 341 55.9
0.87 (0.75, 1.00) 85682 148 24.8 0.045
0.93 (0.81, 1.05) 81582 175 30.8
0.92 (0.76, 1.11) 34426 78 32.5
1.09 (0.92, 1.30) 16806 78 66.8
0.96 (0.83, 1.12) 93490 144 22.1 0.534
0.81 (0.67, 0.98) 48220 79 23.5
0.97 (0.88, 1.08) 78483 262 48.0
1.00 (0.81, 1.25) 38723 65 24.1 0.705
0.84 (0.65, 1.08) 28259 45 22.9
0.95 (0.87, 1.03) 153211 375 35.2
1.00 (0.91, 1.09) 110095 339 44.3 0.009
0.80 (0.69, 0.92) 110098 146 19.0
0.91 (0.79, 1.04) 105765 150 20.3 0.658
0.97 (0.88, 1.06) 112542 322 41.1
0.94 (0.85, 1.03) 161828 326 28.9 0.626
0.94 (0.83, 1.08) 58365 159 39.1
0.89 (0.79, 0.99) 132794 238 25.7 0.066
0.97 (0.84, 1.11) 68252 152 32.0
1.04 (0.87, 1.23) 19147 95 71.2
0.81 (0.64, 1.02) 12385 49 57.4 0.424
0.92 (0.71, 1.19) 7522 34 65.4
0.98 (0.88, 1.08) 118342 272 33.0
0.92 (0.79, 1.08) 81944 130 22.7
0.96 (0.83, 1.10) 115096 139 17.3 0.965
0.93 (0.85, 1.02) 105096 346 47.3
0.95 (0.87, 1.03) 212212 421 28.5 0.834
0.93 (0.76, 1.15) 7553 64 123.7
0.94 (0.91, 0.96)
0.6 0.8 1.0 1.2 1.4

**All-cause mortality**



**CVD mortality**